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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/695,194 | 10/28/2003 | Denis Francois Hochstrasser | A36054-PCT-USA-A<br>072874.0 | 4418 |

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| EXAMINER | |
|---|---|
| SWARTZ, RODNEY P | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/695,194 | HOCHSTRASSER | |
| | Examiner | Art Unit | |
| | Rodney P. Swartz, Ph.D. | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24January2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *20,23-28 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,21,22 and 29-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-47* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



RP

**DETAILED ACTION**

1. Applicants' Response to Restriction Requirement, received 24January2005, is acknowledged.

Applicants elect, with traverse, Invention I, claims 1-19, 21, 22, and 29-46, drawn to a method and kit for diagnosis of TSE by detecting polypeptide, classified in class 436, subclass 501.

The traversal is on the grounds that all of the inventions are clearly connected as being drawn to diagnosis of TSE or related conditions, and have a single, searchable unifying relationship. Therefore, there would not be a serious burden on the examiner for searching and examining the claims as one single application.

This is not found persuasive because of the reasons put forth in the original restriction requirement explanation. While the general subject matter of the claims may be TSE, the various claims are drawn to patentably distinct methods, devices, or normal animals. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-47 are pending. Claims 20, 23-28, and 47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions.

2. Claims 12-19, 21, 22, and 29-46 drawn solely to method and kit for diagnosis of TSE by detecting polypeptide are under consideration.

**Drawings**

3. The drawings are objected to because of the designation of multiple subsets for figures 2-4, 6, 8-10. each figure, e.g., FIG. 2' and Fig. 2". It is recommended that such figures be labeled, e.g., FIG. 2A and Fig. 2B in stead of the current, e.g., FIG. 2' and Fig. 2". A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

**Claim Rejections - 35 USC § 112**

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-10, 16, 19, 21, 22, 37, and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for differentiating between cerebrospinal fluid or plasma from CJD+ and CJD-, plasma of BSE+ and BSE- cattle by measuring very specific molecular weight components of plasma and CSF, does not reasonably provide enablement for method of diagnosis of TSE or BSE utilizing any/all other body fluids nor utilizing any other component having a molecular weight in the range of 1000-100000. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention is a method and kit for the diagnosis of TSE or BSE utilizing any/all body fluids by determining differentially expressed components having a molecular weight in the range of 1000-100000.

The state of the prior art for diagnosis of TSE, BSE and CJD utilizing markers in body fluids is increasing in depth as more research is performed on samples from such hosts (see attached reference). Therefore, there is a lack of predictability in the art concerning identification of such markers without actual experimentation and data collection differentiating between infected and noninfected hosts.

The amount of direction/guidance present in the specification utilizes only CSF and plasma. No other bodily fluids or tissues are utilized. The methodology identifies only two possible markers, cystatin C and isoforms of hemoglobin. The rest of the molecular weight marker components are not identified except by the specific methods utilized in the specification and molecular weight.

The only working examples present in the specification are as follows:

**Example 1:** peaks at 4780, 6700, 8600, and 13,375 Da were significantly differentially *increased* in CSF of CJD-affected patients versus normal CSF.

**Example 2:** peak at 10220 Da significantly *increased* in BSE+ plasma versus BSE- cattle.

**Example 3:** plasma components of 3970, 3990, 4294, 4478, 10,075 11,730, 14,043, and 17,839 were significantly *decreased* in CJD+ plasma versus CJD- patients. Peak at 7770 Da was significantly *increased* in CJD+ plasma versus CJD- plasma.

**Example 4:** plasma components at 3976, 3992, 4300, 4315, 4436, 4484, 6200, 8936, 9107, 9145, 9185, 9454, 10068, 13550, and 17809 Da were decreased in CJD+ patients versus CJD- patients. Plasma components at 7574, 7773, 7930, 7975, and 8020 Da were increased in CJD+ plasma.

**Example 5:** plasma from BSE diagnosed cattle show 23 peaks significantly differentially expressed versus normal cattle plasma. The molecular range was 1010-31,800 Da.

**Example 6:** Cystatin C increased in CSF from CJD+ versus CJD- patients. Molecular weight 13350 Da.

**Example 7:** Isoform of bovine hemoglobin, mw 15000 Da, was increased in plasma from BSE+ versus BSE- cattle.

Thus, the only component markers shown to be differentially expressed as an *increase* range from 1010-31,800 Da molecular weight. The only component markers shows to be differentially expressed as a *decrease* range from 3976-17809 Da.

The quantity of experimentation necessary for the scope of the claims, i.e., a method of diagnosing TSE or BSE constitutes merely an invitation to experiment without a reasonable expectation of

success due the nonidentity of the markers except by molecular weight, lack of indication that such differential expression occurs in any other body fluids or tissues, and a lack of any data indicating markers less than 1010 or greater than 31800 are differentially expressed in TSE+, BSE+, or CJD+ samples.

6. Claims 1-19, 21, 22, and 29-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a method of diagnosis, prognosis, or therapy of TSE by assaying a body fluid or tissue for a polypeptide which is differentially contained in the body fluid of TSE infected compared to a body fluid of TSE noninfected subjects, and "determining whether the test amount is consistent with a diagnosis of TSE".

The claims are indefinite because they appear to be drawn to a method of diagnosis of TSE after "determining whether the test amount is consistent with a diagnosis of TSE". However, in order to determine if the test amount is consistent with a diagnosis of TSE, one has to already have a diagnosis of TSE. Thus, the claims appear to be only drawn to a method of correlating a differential component amount with an already determined diagnosis of TSE.

7. Claims 1-19, 21, 22, and 29-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a method of diagnosis, prognosis, or therapy of TSE by assaying a body fluid or tissue for a polypeptide which is differentially contained in the body fluid of TSE infected compared to a body fluid of TSE noninfected subjects, and determining whether the test amount is consistent with a diagnosis of TSE.

The specification teaches only two actual polypeptides, hemoglobulin isoform and cystatin C. The rest of the component markers only have a molecular weight designation. Therefore, it is unclear

whether all of the other components differentially contained in the tested samples are actually polypeptides.

**Conclusion**

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rodney P. Swartz, Ph.D., Art Unit 1645, whose telephone number is (571) 272-0865. The examiner can normally be reached on Monday through Thursday from 5:30 AM to 4:00 PM EST.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F. Smith, can be reached on (571)272-0864.

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER
Art Unit 1645

April 30, 2005